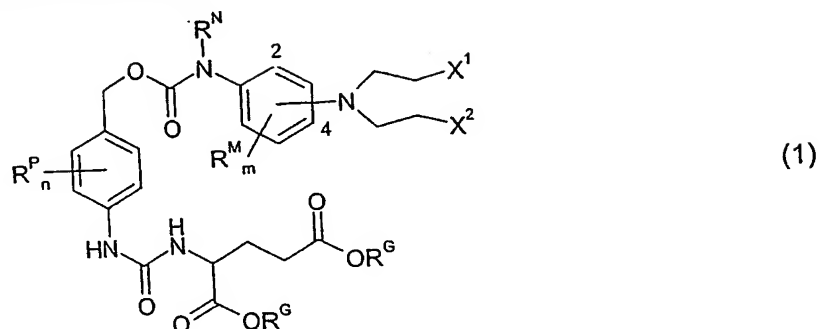


CLAIMS

1. A compound of the formula:



5 wherein:

R^N is independently C_{1-7} alkyl;

X^1 is independently -I, -Br, or -Cl;

X^2 is independently -I, -Br, or -Cl;

the group $-N(CH_2CH_2X^1)(CH_2CH_2X^2)$ is independently attached at the

10 2-position or at the 4-position;

each R^G is independently -H or an ester substituent;

n is independently an integer from 0 to 4;

each R^P , if present, is independently a phenyl substituent;

m is independently an integer from 0 to 4;

15 each R^M , if present, is independently a mustard substituent;

and pharmaceutically acceptable salts, solvates, amides, and esters thereof.

* * *

- 20 2. A compound according to claim 1, wherein R^N is independently aliphatic C_{1-7} alkyl.
3. A compound according to claim 1, wherein R^N is independently unsubstituted C_{1-7} alkyl.
- 25 4. A compound according to claim 1, wherein R^N is independently unsubstituted aliphatic C_{1-7} alkyl.
5. A compound according to claim 1, wherein R^N is independently C_{1-4} alkyl.
- 30 6. A compound according to claim 1, wherein R^N is independently aliphatic C_{1-4} alkyl.

- 94 -

7. A compound according to claim 1, wherein R^N is independently unsubstituted C_{1-4} alkyl.
- 5 8. A compound according to claim 1, wherein R^N is independently unsubstituted aliphatic C_{1-4} alkyl.
9. A compound according to claim 1, wherein R^N is independently -Me, -Et, -nPr, -iPr, -allyl, -nBu, -sBu, -iBu, or -tBu.
- 10 10. A compound according to claim 1, wherein R^N is independently -Me or -Et.
11. A compound according to claim 1, wherein R^N is independently -Me.

15

* * *

12. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -I, -Br, or -Cl; and both of X^1 and X^2 are the same.
- 20 13. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -I or -Br.
14. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -I or -Br; and both of X^1 and X^2 are the same.
- 25 15. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -I.
16. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -Br.
- 30 17. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -Cl.

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* * *

- 95 -

18. A compound according to claim 1, wherein
R^N is independently C₁₋₄alkyl; and,
each X is independently -Cl, -Br or -I.
- 5 19. A compound according to claim 1, wherein
R^N is independently -Et or -Me; and,
each X is independently -Cl, -Br or -I.
- 10 20. A compound according to claim 1, wherein
R^N is independently -Me; and,
each X is independently -Cl, -Br or -I.
- 15 21. A compound according to claim 1, wherein
R^N is independently C₁₋₄alkyl; and,
each X is independently -Br or -I.
22. A compound according to claim 1, wherein
R^N is independently -Et or -Me; and,
each X is independently -Br or -I.
- 20 23. A compound according to claim 1, wherein
R^N is independently -Me; and,
each X is independently -Br or -I.
- 25 24. A compound according to claim 1, wherein
R^N is independently C₁₋₄alkyl; and,
each X is independently -I.
- 30 25. A compound according to claim 1, wherein
R^N is independently -Et or -Me; and,
each X is independently -I.
- 35 26. A compound according to claim 1, wherein
R^N is independently -Me; and,
each X is independently -I.

* * *

- 96 -

27. A compound according to any one of claims 1 to 26, wherein the group $-N(CH_2CH_2X^1)(CH_2CH_2X^2)$ is independently attached at the 4-position.

* * *

- 5 28. A compound according to claim 1, wherein
 R^N is independently C_{1-4} alkyl;
 each X is independently -Cl, -Br or -I; and,
 the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.
- 10 29. A compound according to claim 1, wherein
 R^N is independently -Et or -Me;
 each X is independently -Cl, -Br or -I; and,
 the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.
- 15 30. A compound according to claim 1, wherein
 R^N is independently -Me;
 each X is independently -Cl, -Br or -I; and,
 the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.
- 20 31. A compound according to claim 1, wherein
 R^N is independently C_{1-4} alkyl;
 each X is independently -Br or -I; and,
 the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.
- 25 32. A compound according to claim 1, wherein
 R^N is independently -Et or -Me;
 each X is independently -Br or -I; and,
 the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.
- 30 33. A compound according to claim 1, wherein
 R^N is independently -Me;
 each X is independently -Br or -I; and,
 the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.
- 35

- 97 -

34. A compound according to claim 1, wherein
R^N is independently C₁₋₄alkyl;
each X is independently -I; and,
the group -N(CH₂CH₂X)₂ is independently attached at the 4-position.

35. A compound according to claim 1, wherein
R^N is independently -Et or -Me;
each X is independently -I; and,
the group -N(CH₂CH₂X)₂ is independently attached at the 4-position.

36. A compound according to claim 1, wherein
R^N is independently -Me;
each X is independently -I; and,
the group -N(CH₂CH₂X)₂ is independently attached at the 4-position.

* * *

37. A compound according to any one of claims 1 to 36, wherein n is 0, 1, or 2.

38. A compound according to any one of claims 1 to 36, wherein n is 0 or 1.

39. A compound according to any one of claims 1 to 36, wherein n is 2.

40. A compound according to any one of claims 1 to 36, wherein n is 1.

41. A compound according to any one of claims 1 to 36, wherein n is 0.

* * *

42. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently halo, C₁₋₄alkyl, nitro, or cyano.

43. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently:

-F, -Cl, -Br, -I, -Me, -Et, -nPr, -iPr, -nBu, -sBu, -iBu, -tBu, -NO₂, or -CN.

44. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently -F, -Cl, -Br, or -I.

45. A compound according to any one of claims 1 to 41, wherein each R^P , if present, is independently -F, -Cl or -Br.

5 46. A compound according to any one of claims 1 to 41, wherein each R^P , if present, is independently -F or -Cl.

47. A compound according to any one of claims 1 to 41, wherein each R^P , if present, is independently -F or -Br.

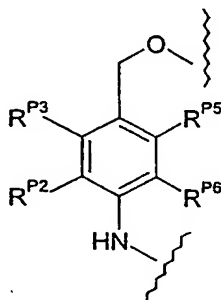
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48. A compound according to any one of claims 1 to 41, wherein each R^P , if present, is independently -F.

* * *

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49. A compound according to any one of claims 1 to 48, wherein the phenylene group has the following formula:



20

wherein each of R^{P2} , R^{P3} , R^{P5} , and R^{P6} is independently -H, halo, C_{1-4} alkyl, nitro, or cyano.

50. A compound according to claim 49, wherein each of R^{P2} and R^{P6} is -H; and each of R^{P3} and R^{P5} is independently halo, C_{1-4} alkyl, nitro, or cyano.

25

51. A compound according to claim 49, wherein each of R^{P2} , R^{P5} , and R^{P6} is -H; and R^{P3} is independently halo, C_{1-4} alkyl, nitro, or cyano.

52. A compound according to claim 49, wherein each of R^{P2} , R^{P3} , R^{P5} , and R^{P6} is -H.

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* * *

- 99 -

53. A compound according to any one of claims 1 to 52, wherein m is 0, 1, or 2.

54. A compound according to any one of claims 1 to 52, wherein m is 0 or 1.

5 55. A compound according to any one of claims 1 to 52, wherein m is 2.

56. A compound according to any one of claims 1 to 52, wherein m is 1.

57. A compound according to any one of claims 1 to 52, wherein m is 0.

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* * *

58. A compound according to any one of claims 1 to 57, wherein each R^M, if present, is independently selected from: C₁₋₄alkyl; C₁₋₄alkoxy; amino; halo; C₁₋₄alkylthio; acyl; ester; amido; cyano; nitro; and, C₅₋₆aryl.

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59. A compound according to any one of claims 1 to 57, wherein each R^M, if present, is independently selected from:

-Me, -Et, -nPr, -iPr, -nBu, -sBu, -iBu, -tBu;
-CF₃, -CH₂F, -CH₂CF₃, -CH₂CH₂F; -CF₂CF₃;
-OMe, -OEt, -O-nPr, -O-iPr, -O-nBu, -O-sBu, -O-iBu, -O-tBu;
-OCF₃, -OCH₂F, -OCH₂CF₃, -OCH₂CH₂F; -OCF₂CF₃;
-NH₂, -NMe₂, -NEt₂, -N(nPr)₂, -N(iPr)₂,
-F, -Cl, -Br, -I;
-SMe, -SEt;
-C(=O)Me;
-C(=O)OMe, -C(=O)OEt;
-CONH₂, -CONHMe;
-CN;
-NO₂; and,
-Ph.

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60. A compound according to any one of claims 1 to 57, wherein each R^M, if present, is independently selected from:

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C₁₋₄alkyl; C₁₋₄alkoxy; and, amino.

- 100 -

61. A compound according to any one of claims 1 to 57, wherein each R^M , if present, is independently selected from:

-Me, -Et, -nPr, -iPr, -nBu, -sBu, -iBu, -tBu;
-CF₃, -CH₂F, -CH₂CF₃, -CH₂CH₂F; -CF₂CF₃;
-OMe, -OEt, -O-nPr, -O-iPr, -O-nBu, -O-sBu, -O-iBu, -O-tBu;
-OCF₃, -OCH₂F, -OCH₂CF₃, -OCH₂CH₂F; -OCF₂CF₃;
-NH₂, -NMe₂, -NEt₂, -N(nPr)₂, and -N(iPr)₂,

62. A compound according to any one of claims 1 to 57, wherein each R^M , if present, is independently selected from:

-Me, -Et, -CF₃, -OMe, -OEt, -NH₂, and -NMe₂.

* * *

63. A compound according to any one of claims 1 to 62, wherein each R^G is independently -H.

* * *

64. A compound according to any one of claims 1 to 62, wherein each R^G is independently -H, unsubstituted C₁₋₇alkyl, substituted C₁₋₇alkyl, or silyl.

65. A compound according to any one of claims 1 to 62, wherein each R^G is independently -H, unsubstituted C₁₋₇alkyl, or substituted C₁₋₇alkyl.

66. A compound according to any one of claims 1 to 62, wherein each R^G is independently -H or unsubstituted C₁₋₇alkyl.

* * *

67. A compound according to any one of claims 64 to 66, wherein the unsubstituted C₁₋₇alkyl group is independently unsubstituted C₁₋₄alkyl.

68. A compound according to any one of claims 64 to 66, wherein the unsubstituted C₁₋₇alkyl group is independently: -Me, -Et, -nPr, -iPr, -allyl, -nBu, -sBu, -iBu, or -tBu.

* * *

69. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁₋₇alkyl substituted with one or more groups selected from optionally substituted C₅₋₂₀aryl, C₁₋₇alkoxy, C₁₋₇alkylthio, and acyloxy.
- 5 70. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁₋₄alkyl substituted with one or more groups selected from optionally substituted C₅₋₂₀aryl, C₁₋₇alkoxy, C₁₋₇alkylthio, and acyloxy.
- 10 71. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁alkyl substituted with one or more groups selected from optionally substituted C₅₋₂₀aryl, C₁₋₇alkoxy, C₁₋₇alkylthio, and acyloxy.
- 15 72. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁₋₇alkyl substituted with one or more groups selected from optionally substituted C₅₋₆aryl, C₁₋₄alkoxy, C₁₋₄alkylthio, C₁₋₄alkyl-acyloxy, C₅₋₆aryl-acyloxy.
- 20 73. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁₋₄alkyl substituted with one or more groups selected from optionally substituted C₅₋₆aryl, C₁₋₄alkoxy, C₁₋₄alkylthio, C₁₋₄alkyl-acyloxy, C₅₋₆aryl-acyloxy.
- 25 74. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁alkyl substituted with one or more groups selected from optionally substituted C₅₋₆aryl, C₁₋₄alkoxy, C₁₋₄alkylthio, C₁₋₄alkyl-acyloxy, C₅₋₆aryl-acyloxy.
- 30 75. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁₋₇alkyl substituted with one or more groups selected from optionally substituted phenyl (e.g., methoxyphenyl, nitrophenyl), methoxy, methylthio, acetoxy, and benzoyloxy.
- 35 76. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁₋₄alkyl substituted with one or more groups selected from optionally substituted phenyl (e.g., methoxyphenyl, nitrophenyl), methoxy, methylthio, acetoxy, and benzoyloxy.

- 102 -

77. A compound according to claim 64 or claim 65, wherein the substituted C₁₋₇alkyl group is independently C₁alkyl substituted with one or more groups selected from optionally substituted phenyl (e.g., methoxyphenyl, nitrophenyl), methoxy, methylthio, acetoxy, and benzoyloxy.

5

* * *

78. A compound according to claim 64, wherein the silyl group is independently -SiR^S₃, wherein each R^S is independently -H or C₁₋₄alkyl.

10

79. A compound according to claim 64, wherein the silyl group is independently -Si(Me)₃, -Si(Et)₃, -Si(iPr)₃, -Si(tBu)(CH₃)₂, or -Si(tBu)₃.

80. A compound according to claim 64, wherein the silyl group is independently -Si(iPr)₃.

15

* * *

81. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) t-butyl, (2) allyl, (3) tri-isopropylsilyl, (4) acetoxymethyl, (5) methoxymethyl, (6) methylthiomethyl, (7) p-methoxyphenylmethyl, (8) bis(o-nitrophenyl)methyl, (9) benzyl, or (10) diphenylmethyl.

20

82. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) t-butyl, (2) allyl, (3) tri-isopropylsilyl, (4) acetoxymethyl, or (5) methoxymethyl.

25

83. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) t-butyl, (2) allyl, or (3) tri-isopropylsilyl.

30

84. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) t-butyl or (2) allyl.

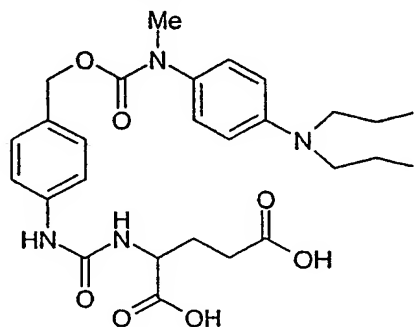
85. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) allyl.

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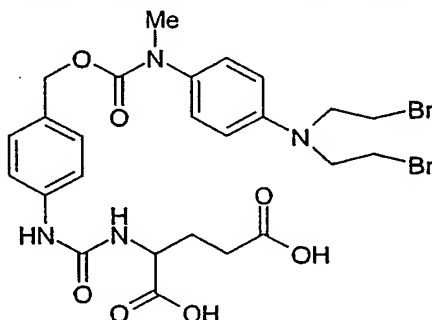
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- 103 -

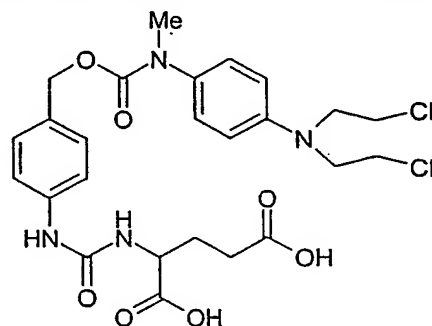
86. A compound selected from compounds of the following formula (P-1), and pharmaceutically acceptable salts, solvates, amides, and esters thereof:



- 5 87. A compound selected from compounds of the following formula (P-2), and pharmaceutically acceptable salts, solvates, amides, and esters thereof:



88. A compound selected from compounds of the following formula (P-3), and pharmaceutically acceptable salts, solvates, amides, and esters thereof:



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* * *

- 15 89. A composition comprising a compound according to any one of claims 1 to 88, and a carrier.
90. A composition comprising a compound according to any one of claims 1 to 88, and a pharmaceutically acceptable carrier.

- 104 -

* * *

5 91. A method of (a) regulating proliferation of a cell; (b) inhibiting cell cycle progression of a cell; (c) promoting apoptosis of a cell; or (d) a combination of one or more of these, *in vitro* or *in vivo*, comprising contacting the cell with an effective amount of a compound according to any one of claims 1 to 90.

10 92. A method of regulating proliferation of a cell, *in vitro* or *in vivo*, comprising contacting the cell with an effective amount of a compound according to any one of claims 1 to 90.

15 93. A method of treatment of a proliferative condition comprising administering to a subject in need of treatment a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

20 94. A method of treatment of cancer comprising administering to a subject in need of treatment a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

* * *

25 95. A compound according to any one of claims 1 to 90, for use in a method of treatment of the human or animal body by therapy.

96. A compound according to any one of claims 1 to 90, for use in a method of treatment of a proliferative condition of the human or animal body by therapy.

30 97. A compound according to any one of claims 1 to 90, for use in a method of treatment of cancer of the human or animal body by therapy.

* * *

35 98. Use of a compound according to any one of claims 1 to 90 for the manufacture of a medicament for the treatment of a proliferative condition.

99. Use of a compound according to any one of claims 1 to 90 for the manufacture of a medicament for the treatment of cancer.

- 105 -

* * *

100. A kit comprising:

- 5 (a) a compound according to any one of claims 1 to 90; and
 (b) instructions for use.

* * *

10 101. A method of (a) regulating proliferation of a cell; (b) inhibiting cell cycle
progression of a cell; (c) promoting apoptosis of a cell; or (d) a combination of one
or more of these, *in vitro* or *in vivo*, comprising contacting the cell with a
therapeutically-effective amount of a compound according to any one of claims 1
to 90, in the presence of a carboxypeptidase enzyme.

15

102. A method of regulating proliferation of a cell, *in vitro* or *in vivo*, comprising
contacting the cell with a therapeutically-effective amount of a compound
according to any one of claims 1 to 90, in the presence of a carboxypeptidase
enzyme.

20

103. A method of treatment of a proliferative condition comprising administering to a
subject in need of treatment a therapeutically-effective amount of a compound
according to any one of claims 1 to 90, in the presence of a carboxypeptidase
enzyme.

25

104. A method of treatment of cancer comprising administering to a subject in need of
treatment a therapeutically-effective amount of a compound according to any one
of claims 1 to 90, in the presence of a carboxypeptidase enzyme.

30

* * *

105. A two component system comprising:

- (a) a compound according to any one of claims 1 to 90; and,
 (b) an antibody or fragment thereof conjugated or fused to a
35 carboxypeptidase enzyme.

- 106 -

106. A two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) an antibody or fragment thereof conjugated or fused to a
carboxypeptidase enzyme,

5 for use in a method of treatment of the human or animal body by therapy.

* * *

107. Use of a two component system comprising:

10 (a) a compound according to any one of claims 1 to 90; and,

(b) an antibody or fragment thereof conjugated or fused to a
carboxypeptidase enzyme,

for the manufacture of a medicament for the treatment of a proliferative condition.

15 108. Use of a two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) an antibody or fragment thereof conjugated or fused to a
carboxypeptidase enzyme,

for the manufacture of a medicament for the treatment of cancer.

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* * *

109. A kit comprising:

(a) a compound according to any one of claims 1 to 90;

25 (b) an antibody or fragment thereof conjugated or fused to a
carboxypeptidase enzyme; and,

(c) instructions for use.

* * *

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110. A method of (a) regulating proliferation of a cell; (b) inhibiting cell cycle
progression of a cell; (c) promoting apoptosis of a cell; or (d) a combination of one
or more of these, *in vitro* or *in vivo*, comprising:

35 (i) contacting the cell with an antibody or fragment thereof conjugated or
fused to a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a
compound according to any one of claims 1 to 90.

111. A method of regulating proliferation of a cell, *in vitro* or *in vivo*, comprising:
(i) contacting the cell with an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme; and,
(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.
112. A method of treatment of a proliferative condition, comprising administering to a subject in need of treatment:
(i) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme; and,
(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.
113. A method of treatment of cancer, comprising administering to a subject in need of treatment:
(i) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme; and,
(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

* * *

114. A two component system comprising:
(a) a compound according to any one of claims 1 to 90; and,
(b) a nucleic acid encoding a carboxypeptidase enzyme.
115. A two component system comprising:
(a) a compound according to any one of claims 1 to 90; and,
(b) a nucleic acid encoding a carboxypeptidase enzyme,
for use in a method of treatment of the human or animal body by therapy.

* * *

116. Use of a two component system comprising:
(a) a compound according to any one of claims 1 to 90; and,
(b) a nucleic acid encoding a carboxypeptidase enzyme,
for the manufacture of a medicament for the treatment of a proliferative condition.

117. Use of a two component system comprising:

- (a) a compound according to any one of claims 1 to 90; and,
 - (b) a nucleic acid encoding a carboxypeptidase enzyme,
- for the manufacture of a medicament for the treatment of cancer.

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* * *

118. A kit comprising:

- (a) a compound according to any one of claims 1 to 90;
- (b) a nucleic acid encoding a carboxypeptidase enzyme; and,
- (c) instructions for use.

10

* * *

119. A method of (a) regulating proliferation of a cell; (b) inhibiting cell cycle progression of a cell; (c) promoting apoptosis of a cell; or (d) a combination of one or more of these, *in vitro* or *in vivo*, comprising:

15

(i) contacting the cell with a nucleic acid encoding a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

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120. A method of regulating proliferation of a cell, *in vitro* or *in vivo*, comprising:

(i) contacting the cell with a nucleic acid encoding a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

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121. A method of treatment of a proliferative condition, comprising administering to a subject in need of treatment:

(i) a nucleic acid encoding a carboxypeptidase enzyme; and,

(ii) a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

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122. A method of treatment of cancer, comprising administering to a subject in need of treatment:

(i) a nucleic acid encoding a carboxypeptidase enzyme; and,

(ii) a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

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